Funding Opportunity: Assays for High-Throughput Screening in the Molecular Libraries Probe Production Centers Network

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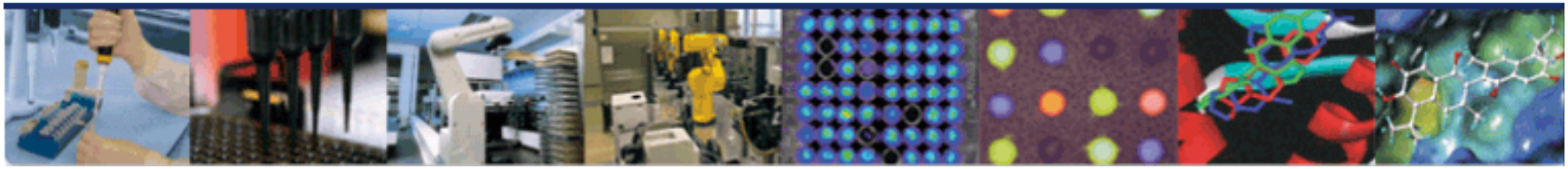


Chemical Probes to Perturb Cell Signaling

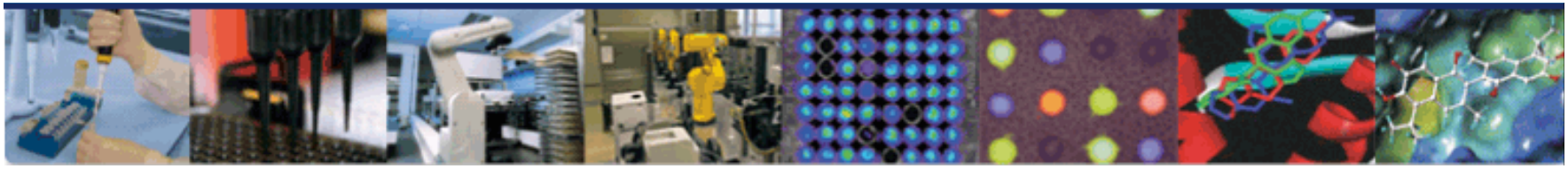
siRNA

- Gene-specific loss of function of whole protein;
- Relatively slow action (hrs to days)

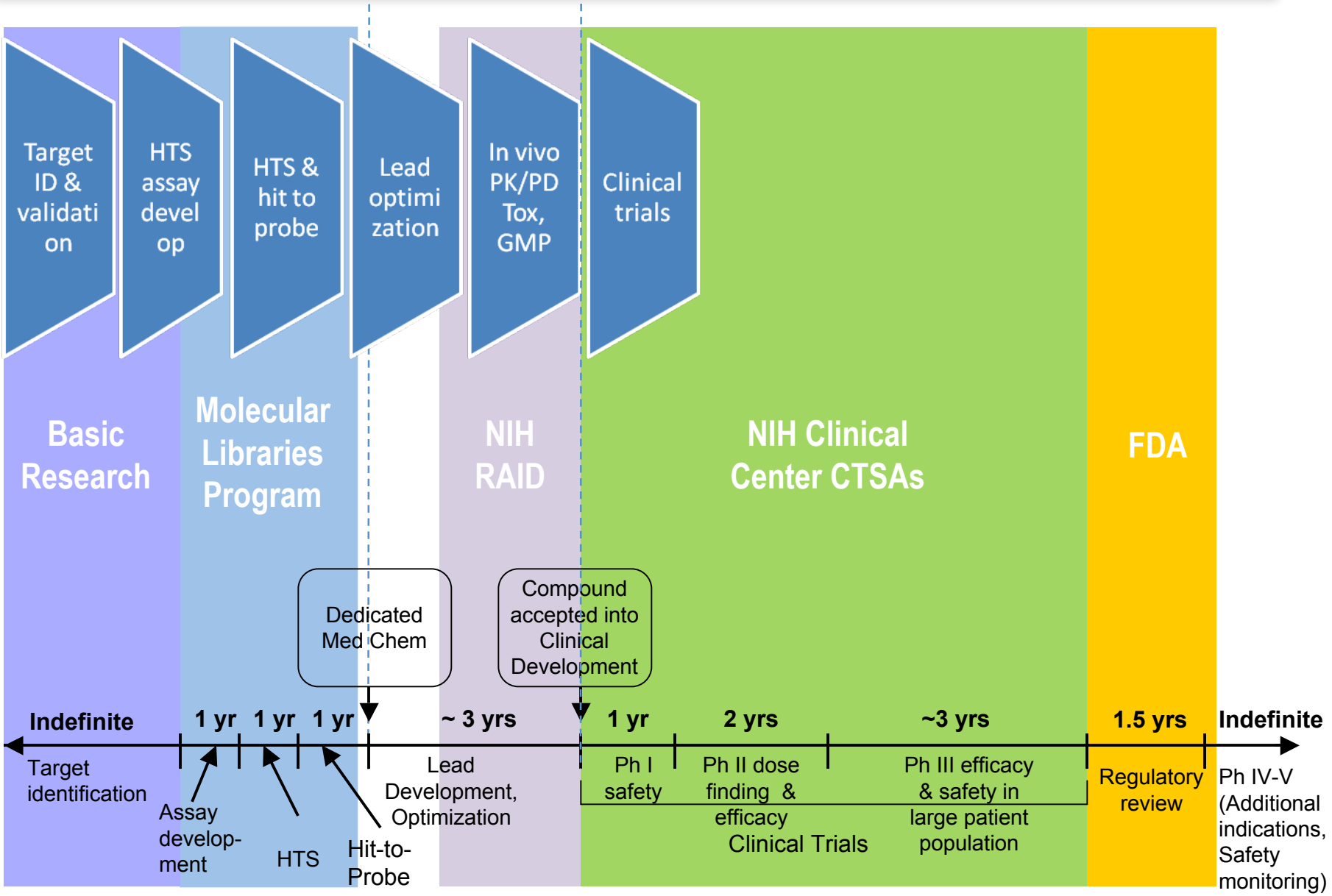
Chemical

- Graded modulation via binding (+/- etc);
- Rapid and reversible action;
- Tissue penetration

76 probe reports by September 2009
https://mli.nih.gov/mli/mlp-probes/



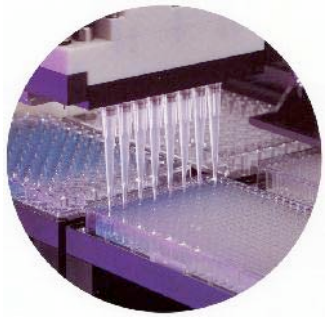
Chemical Probes for Drug Discovery



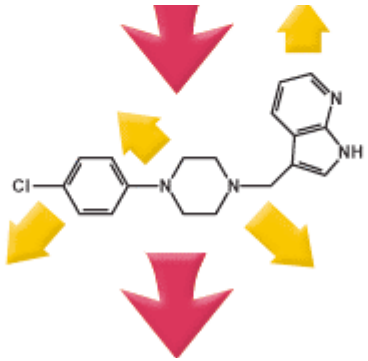
Molecular Libraries Program is a Multidisciplinary Team Effort

HTS Assays from the Community

Compounds from the SMR

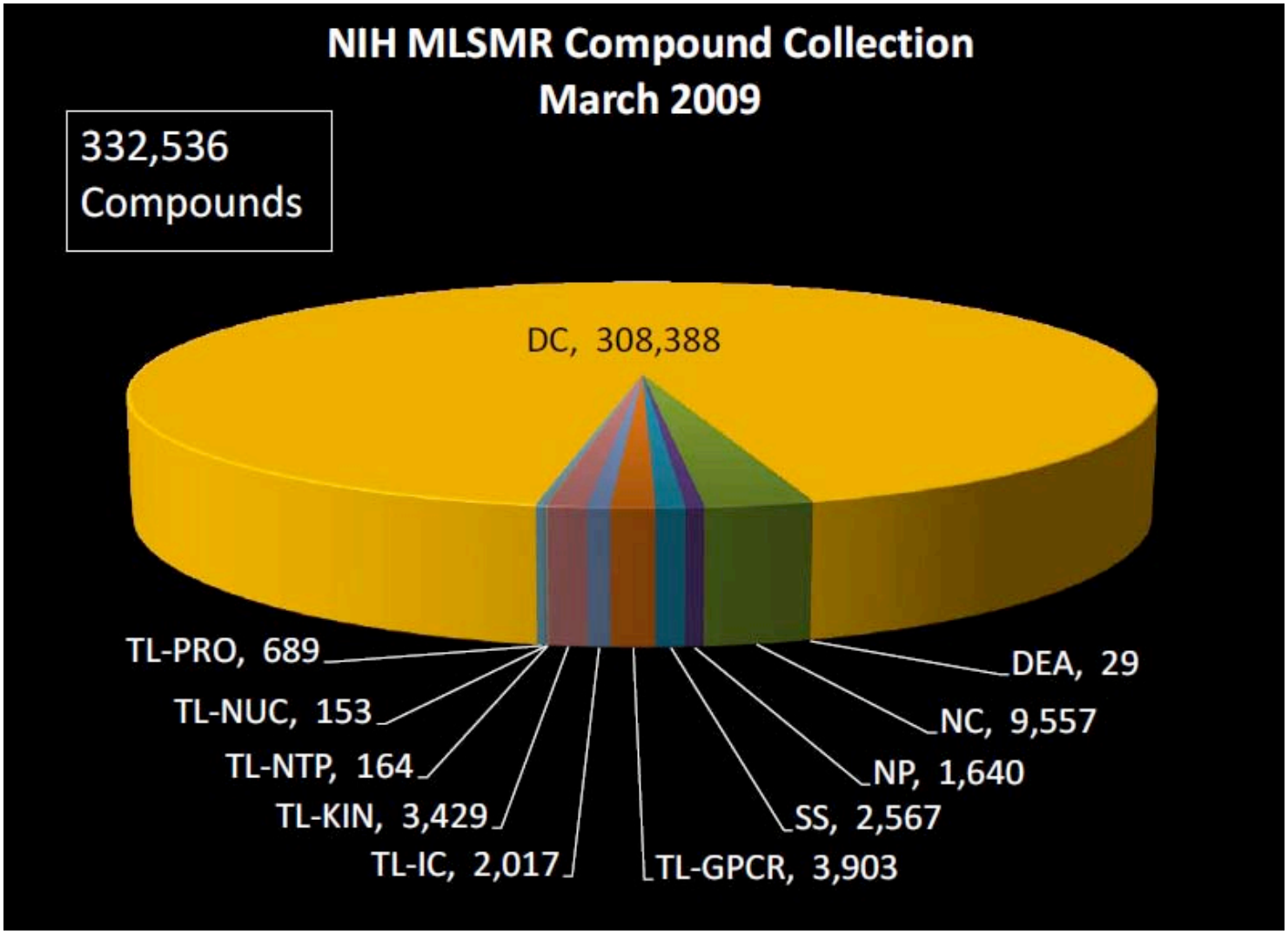


MLPCN Screening Centers Network



PubChem

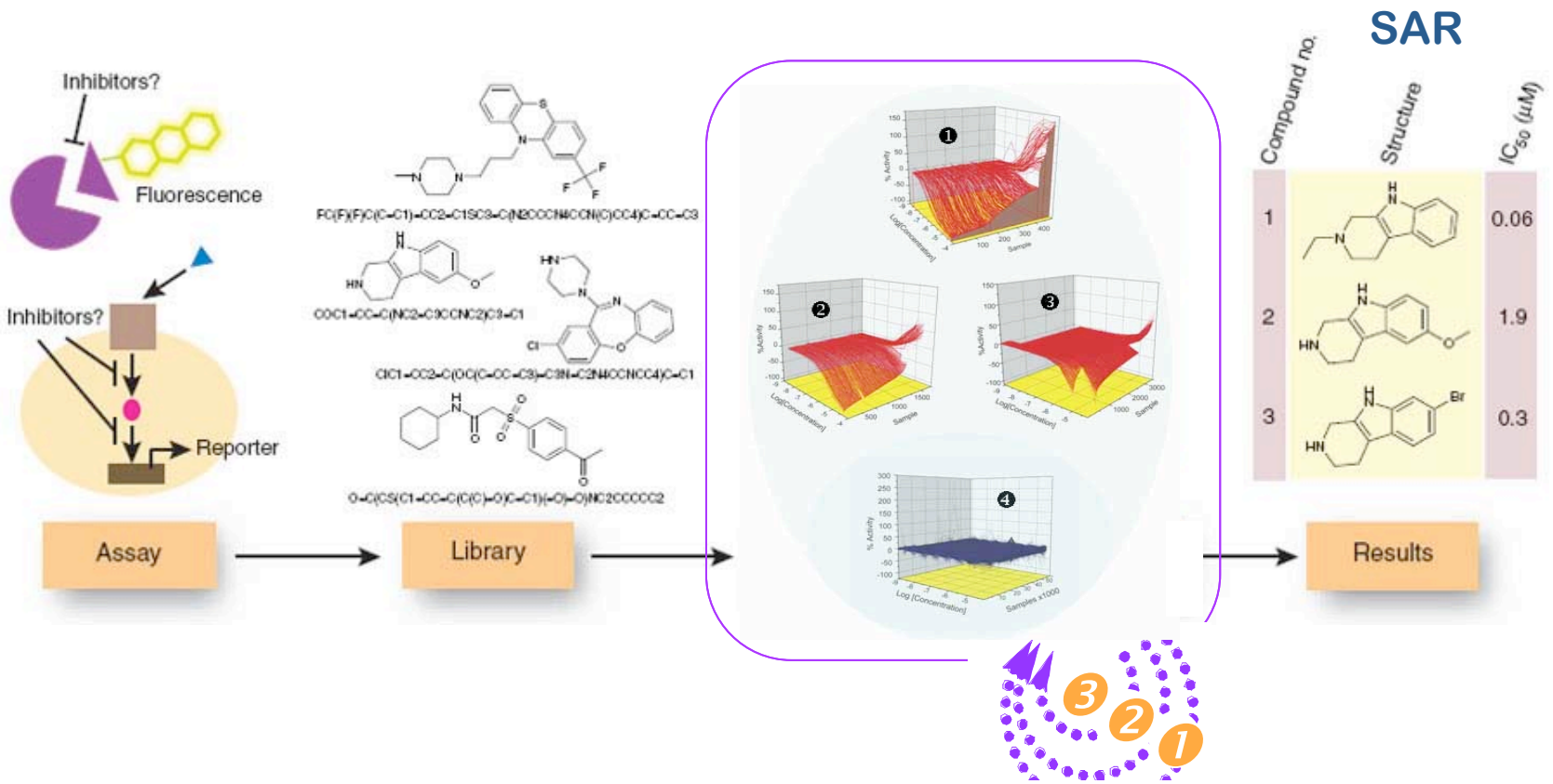
NATIONAL INSTITUTES OF HEALTH



DC = Diversity Compound Set
NC = Non-commercial
TL-KIN = Kinase Targeted Library
TL-GPCR = GPCR Targeted Library
TL-IC = Ion Channel Targeted Library

TL-PRO = Protease Targeted Library
TL-NUC = Nuclear Receptor Targeted
TL-NTP = National Toxicology Program
SS = Known Bioactives
NP = Natural Products
DEA = DEA Controlled Substances

HTS Methods to Develop Chemical Probes



Courtesy of NCGC

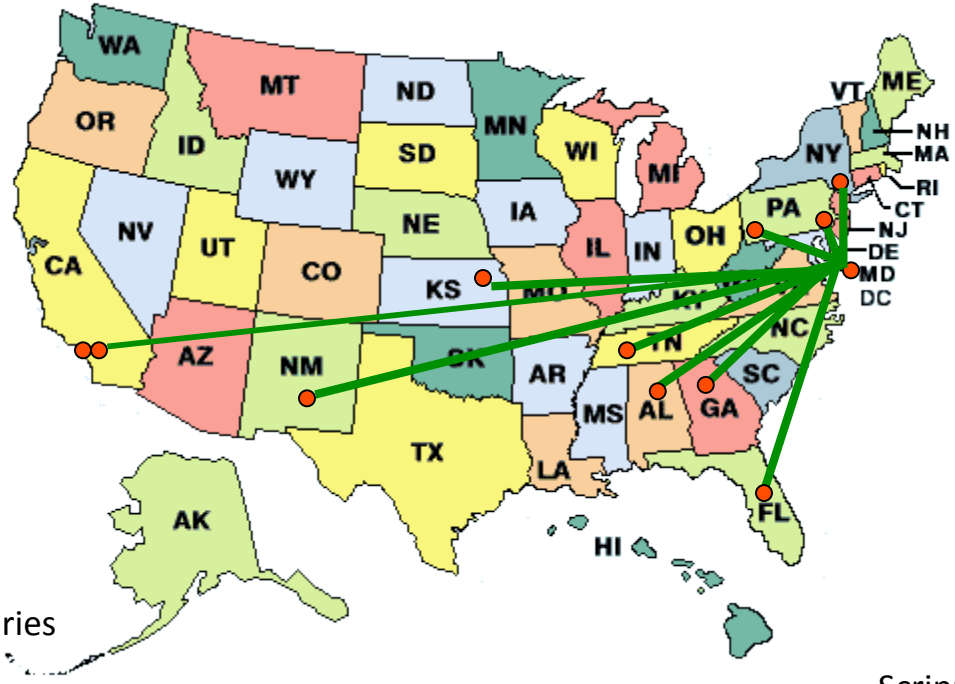
NIH Molecular Libraries Probe Production Center Network (MLPCN)

University of Kansas Chemistry Center

Scripps Research Institute Molecular Screening Center

Burnham Institute for Chemical Genomics

New Mexico Molecular Libraries Screening Center



Broad Institute Comprehensive Screening Center

John Hopkins Ion Channel Center

NIH Chemical Genomics Center (NCGC)

Vanderbilt Specialized Chemistry Center

Scripps Florida Molecular Screening Center

Southern Research Specialized Biocontainment Screening Center

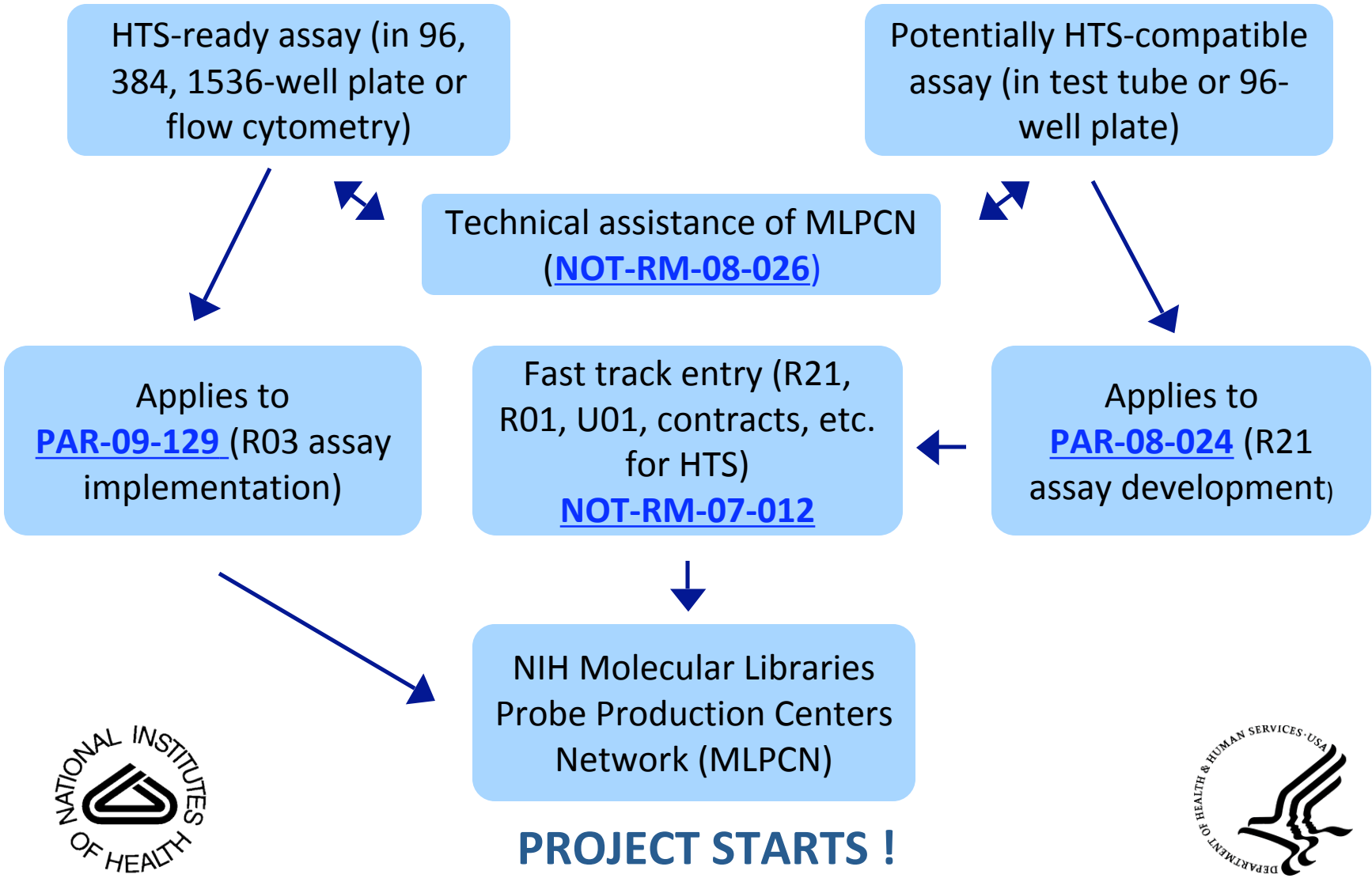
MLPCN Center Capabilities
(visit http://mli.nih.gov/mli/)

- **Comprehensive Centers**
  Burnham, Broad, NCGC, and Scripps –
  Biochemical, cell-based, phenotypic, HCS (microscopic imaging) assays; qHTS, BSL-2, GPCR, nuclear receptor, protein-protein, enzyme, reporter gene, etc. Cheminformatic analyses of hits, SAR expansion (analog by catalog and synthesis),

- **Specialized Screening Centers**
  Johns Hopkins – ion channel, automated patch clamp assays
  U New Mexico – Flow cytometry based multiplex assays for multiple targets;
  Southern Research Institute – BSL-2/3 biocontainment assays

- **Specialized Chemistry Centers**
  Kansas, and Vanderbilt –
  Cheminformatic analyses of hits, SAR expansion (analog by catalog and synthesis), iterative parallel synthesis approach coupled with medicinal chemistry design

How to Access HTS and Chemistry Resources of MLPCN



"On-Ramps" to the MLPCN

❑ Solicitation of Assays for HTS (PAR-09-129)

- 2-year HTS and probe development project (R03)
- $50k (direct costs) provided for MLPCN collaboration
- 3 receipt dates/year (next date: January 4, 2010)

❑ Assay Development for HTS (PAR-08-024)

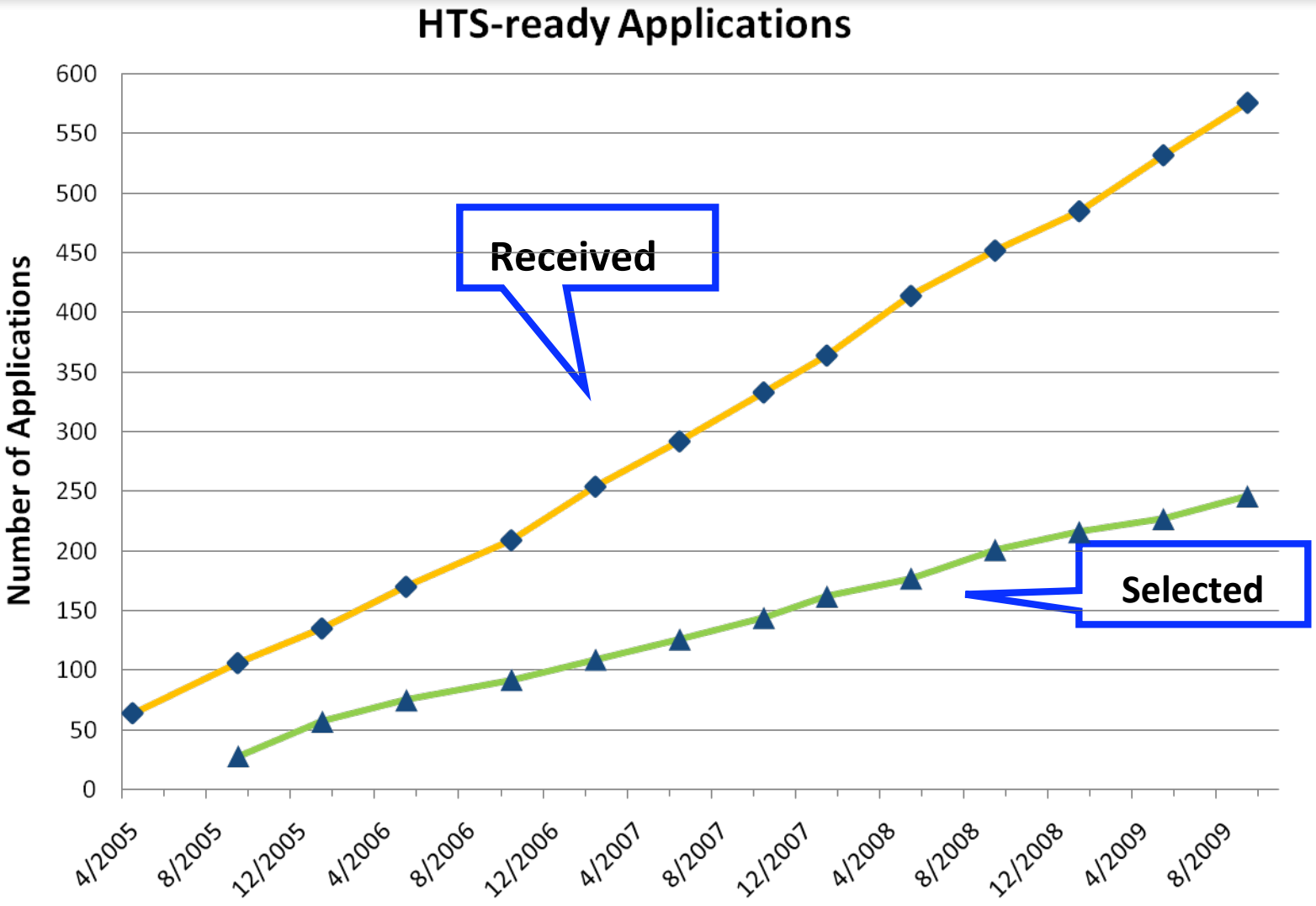
- 1 year upstream of MLPCN entry (R21)
- $100K of funding, expedited entry to the Network when HTS ready, $25k (direct costs) provided for MLPCN collaboration
- 2 receipt dates/year (next date: November 20, 2009)

❑ *Fast Track* entry to the MLPCN (NOT RM-07-012)

- Monthly RM Project Team review
- All NIH grants & Sponsored Programs in which HTS and small molecule probe development is an objective are eligible

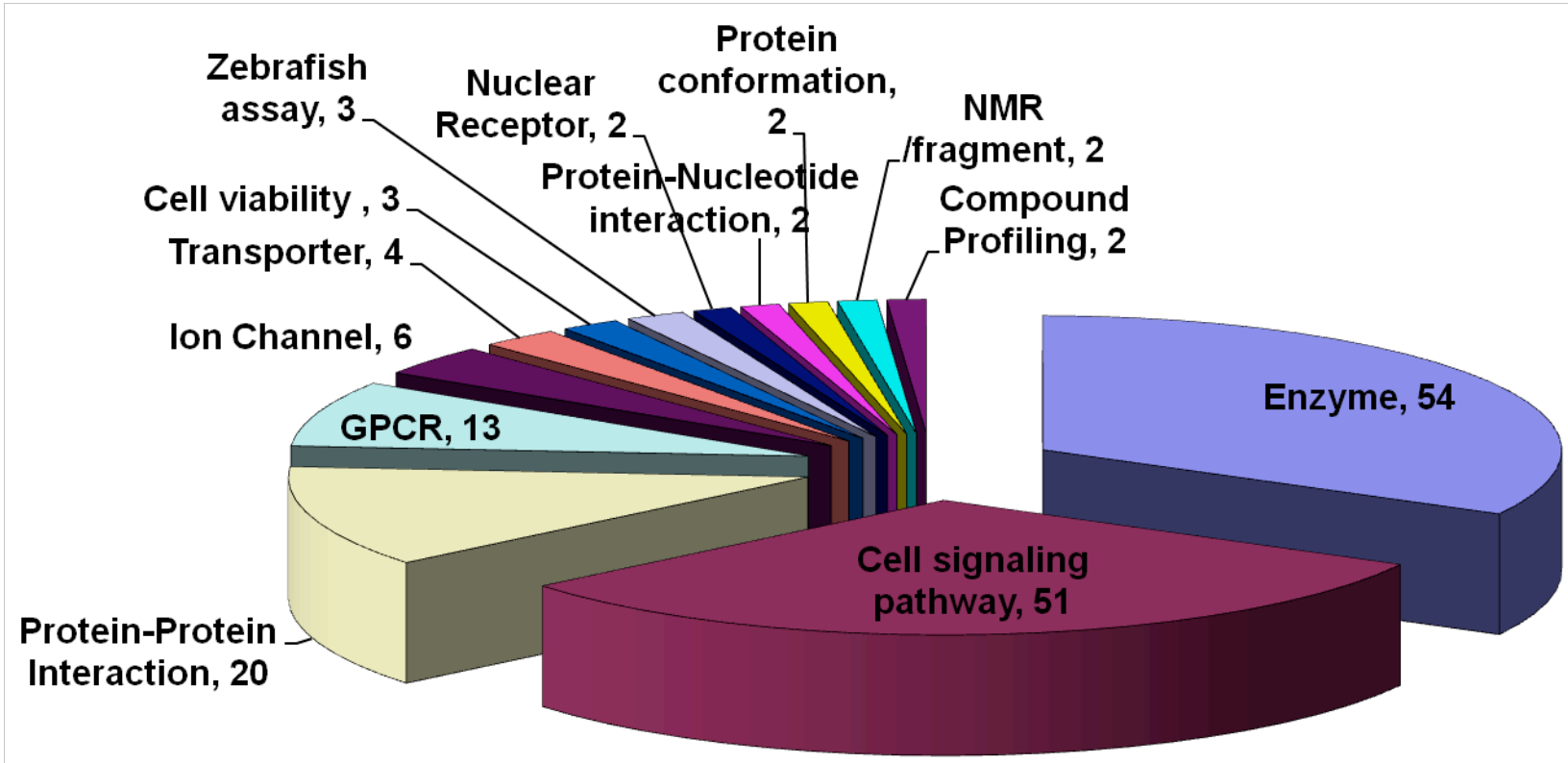
PAR-09-129 HTS-ready Assay Applications (R03)

Received 576 Applications, Awarded 246 Applications

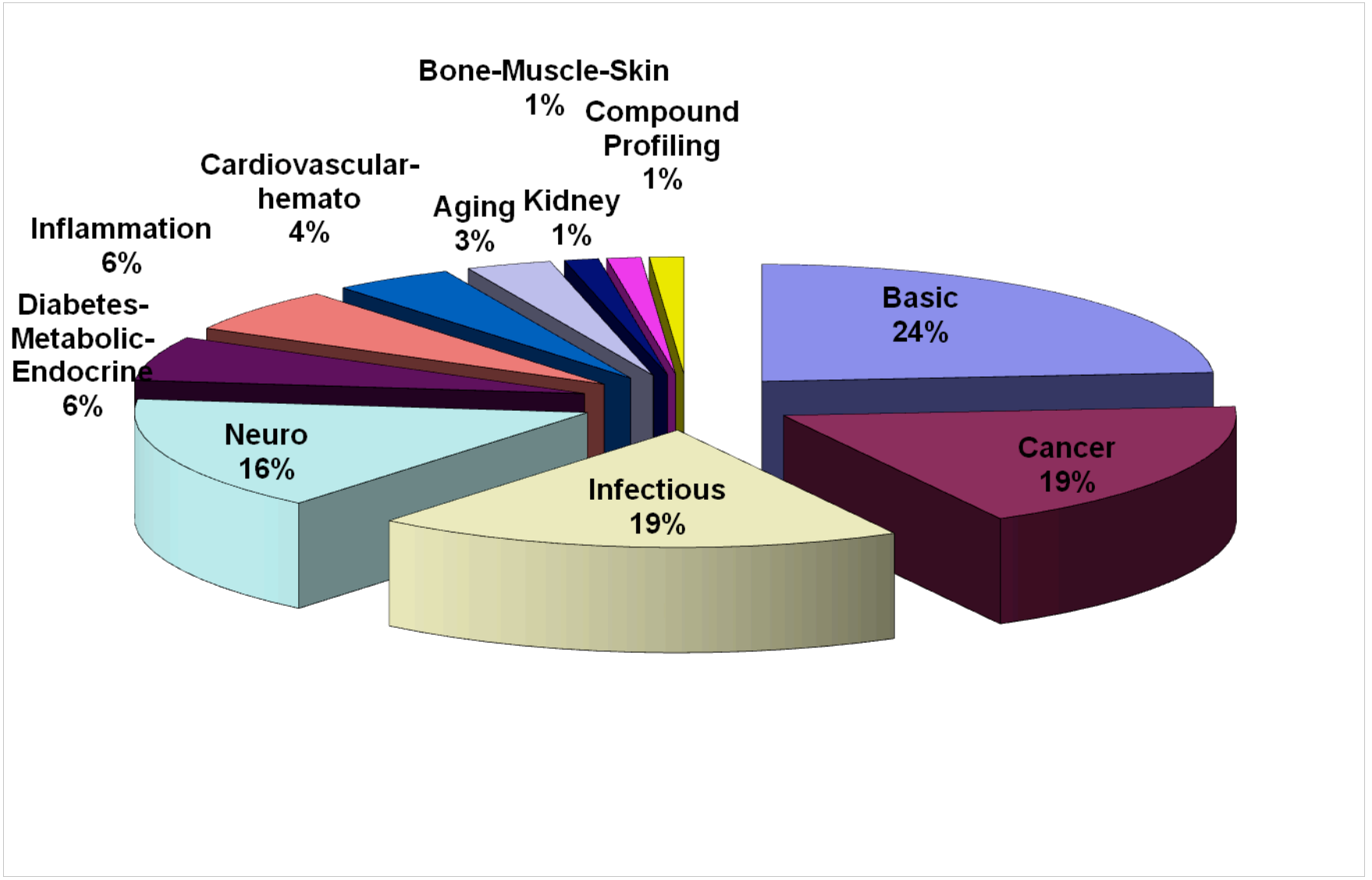


MLP Assay Target Portfolio

164 MLSCN grant projects



Research Fields of MLP Projects (MLSCN)



Guidelines for HTS R03 Applicants

PAR-09-129 (R03)

If you have never applied for an NIH grant, please visit http://era.nih.gov/ElectronicReceipt/index.htm

DON'T DELAY, REGISTER NOW!	Grants.gov			eRA Commons
	CCR registration (requires DUNS #)	Obtain and register Grants.gov credentials	Authorize Organization Rep.	eRA Commons Registration (Org. registration requires DUNS #)
Principal Investigators				X
Institutions/ Organizations	X	X	X	X

Guidelines for HTS R03 Applicants

PAR-09-129 Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Probe Production Centers Network (MLPCN) (R03)

- **Emphasis on significance of targets/phenotypes, especially targets/ phenotypes for which selective and potent small molecule modulators are not available to the public (check PubChem and provide compelling rationale)**

- **Provide preliminary primary assay and hit validation assay data for HTS readiness: Z' ≥0.5 (show plate data with a pilot screen of ~2,000 compounds)**

- **Provide a plan for hit follow-up assays that are crucial for the optimization of chemical probes (e.g. selectivity, cellular activity etc.) or for the determination of mechanisms of action**

Guidelines for HTS R03 Applicants

PAR-09-129 Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Probe Production Centers Network (MLPCN) (R03)

- **For technical assistance by Center staff, please submit an online form:**

  http://mli.nih.gov/mli/mlpcn/access-to-technical-assistance-of-mlpcn/tech-assistance-request-form/

- **For HTS assay methodology, view Assay Guidance Manual**

  http://www.ncgc.nih.gov/guidance/index.html

- **For Program assistance, please contact:**

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  301-443-6102

The next submission date is 1/4/2010